

### **REMARKS**

Claims 65-71 were pending prior to this Response, with claims 1-64 and 72 having been canceled in response to a restriction requirement. By the present communication, no claims have been added, claim 66 has been canceled without prejudice, and claim 65 has been amended to recite Applicants' invention with greater particularity. Applicants respectfully request entry of the amendments set forth in this response under 37 CFR §1.116. The amendments do not raise any issues of new matter and the amended claims do not present new issues requiring further consideration or search. Support for the term "individually" in claim 65, may be found, among others, at page 23, lines 15-29, and at page 45, lines 4-7. The claim amendments do not constitute new matter, being fully supported by the Specification and original claims. Accordingly, claims 65 and 67-71 are currently pending in this application.

### **Rejection under 35 U.S.C. § 112, First Paragraph**

Applicants respectfully traverse the rejection under 35 U.S.C. § 112, first paragraph, of claims 65-71 as containing subject matter that was not sufficiently described in the specification as to reasonably convey to those skilled in the art that Applicants were in possession of the invention as claimed. Specifically, the Examiner alleges that "the specification and claims do not place any limit on the number of atoms, the type of atoms, or the manner in which said atoms might be connected to form the microenvironment." (Office Action, page 3). Further, the Examiner alleges that "the specification only teaches "microorganisms" and, as a result, Applicants are not in possession of the broader organisms that are not microorganisms." (Office Action, page 3). Finally, the Examiner alleges that the phrases "two or more organism" and "on the basis of growth of the organism" are new matter and indefinite.

Applicants have canceled claim 66 without prejudice, rendering the rejection moot as pertains to claim 66. Applicants respectfully submit that examples of "microenvironments" are provided throughout the Specification. However, to further prosecution of this application, Applicants have amended claim 65 to recite "an aqueous microenvironment". The term

“microenvironments” is specifically defined as “any molecular structure which provides an appropriate environment for facilitating the interactions necessary for the method of the invention” (Specification, page 24, lines 27-29). Accordingly, Applicants submit that those of skill in the art would have understood the possible aqueous microenvironments for use with the methods of the invention, and that Applicants had possession of the scope of the term at the filing of the application.

With regard to the term “microorganisms,” the specification provides adequate teaching in support of the term “organisms.” For example, the specification specifically discusses “organisms” at, among others, page 1, line 13; page 7, line 29; page 13, line 5; page 13, line 12; page 13, line 29; page 14, line 16; page 14, line 28; page 15, lines 13-16; page 16, line 16; page 17, line 4; page 17, line 17; page 17, line 27; and page 21, line 29. Microorganisms are taught as being one example of a particular organism that is useful in the methods of the invention. Accordingly, Applicants submit that those of skill in the art would have understood that Applicants had possession of the scope of the term “organism” at the time of filing the application.

With regard to the phrase “two or more organism”, Applicants respectfully direct the Examiner’s attention to the Specification at page 17, lines 1-5, which teaches that the methods of the invention may be practiced using “nucleic acid derived from more than organism or source, *e.g.*, a mixed population of organisms.” Support may further be found at page 42, lines 29-31, which teach that the methods of the invention may be practiced using “clones containing selected DNA derived from a mixed population of organisms or more than one organism.” Applicants submit that the phrase “more than one” and “two or more” are equivalent when used in reference to organisms because organisms must be described in whole numbers. Consequently, Applicants respectfully submit that the phrase “two or more organisms” is supported by the Specification as filed, and withdrawal of the rejection is requested.

With regard to the phrase “on the basis of growth,” allegedly being indefinite for including an indefinite number of sorting techniques, Applicants submit that claim 65 has been amended to remove the term “basis” therefrom. Consequently, amended claim 65 describes the technique by which the microenvironments are sorted (i.e., by growth of the organism alone). Accordingly, Applicants submit that amended claim 65 is definite, and withdrawal of the rejection is respectfully requested.

In view of the extensive listing of “representative examples” of the terms used in the claims, Applicants submit that those of skill in the art would understand that the Applicants were “in possession” of the invention as claimed and would have understood their intention at filing of the application that the invention could be practiced in accordance with the full scope of claim 65, rather than being limited to the particular example(s) used to illustrate the invention in the Examples of the Specification.

Accordingly, reconsideration and withdrawal of the rejection of claims under 35 U.S.C. § 112, first paragraph, for allegedly lacking sufficient written description to support the claims are respectfully requested.

**Rejection under 35 U.S.C. § 112, Second Paragraph**

Applicants respectfully traverse the rejection under 35 U.S.C. § 112, second paragraph, of claim 65 as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Specifically, the Examiner alleges that “sorting the microenvironments by a flow cytometer on the basis of growth of the organism” is vague because step (b) requires that the organisms be given adequate time to “grow” and, as a result, all of the cells would be allowed to grow before they were sorted. Further, the Examiner alleges that the limitation “the organisms” and “the organism” in lines 5 and 10 respectively have insufficient antecedent basis.

Applicants have amended claim 65 to define Applicants' invention with greater particularity. As amended, step (b) of claim 65 provides incubating for such time as to allow *at least one* of the organisms to grow. The subsequent sorting is by growth of the organisms alone to separate organisms that grow under the conditions from organisms that do not grow under the conditions. Further, Applicants have amended step (c) to recite: sorting the microenvironments by a flow cytometer on growth of the organisms alone to separate organisms that grow under the conditions from organisms that do not grow under the conditions. Applicants submit that proper antecedent basis now exists for all terms used throughout amended claim 65.

Accordingly, Applicants submit that amended claim 65 is definite as required by 35 U.S.C. § 112, second paragraph, and withdrawal of the rejection is respectfully requested.

**Rejection under 35 U.S.C. § 102(b)**

A. Applicants respectfully traverse the rejection of claims 65-67 under 35 U.S.C. § 102(b) as allegedly being anticipated by Powell et al. (*Biotechnology*, (April 1990) 8,4:333-337).

Applicants have canceled claim 66 without prejudice, rendering the rejection moot as pertains to claim 66. However, Applicants respectfully submit that the invention methods for obtaining an organism from a mixed population of organisms in a sample, as defined by amended claim 65 (and claim 67 dependent therefrom), distinguish over the disclosure of Powell et al. by requiring:

“individually encapsulating two or more organisms obtained from the sample, each in an aqueous microenvironment suitable for growth of the organisms;

incubating the encapsulated organisms under such conditions and for such a time to allow the organisms to grow; and

sorting the microenvironments by a flow cytometer on the basis of growth of the organism to obtain an organism from the sample that grows under the conditions.” It should be noted that Applicants' claims do not require secretion or production of any analyte as the basis of cell separation.

By contrast, Powell et al. fail to disclose encapsulating organisms within a microenvironment, incubating the organisms and then sorting the encapsulated organisms using a flow cytometer to separate cells on the basis of growth of the organisms, i.e., to separate organisms that grow under the incubation conditions from cells that do not grow under the incubation conditions. In fact, Applicants submit that Powell et al. are concerned with using gel microdroplets and flow cytometry, not as an assay for organism growth, but to determine a product secreted from an organism, which product becomes the analyte. Thus Powell et al. fail to disclose at least two elements of claims 65-67.

Anticipation under 35 U.S.C. § 102(b) requires that the reference recite each and every element of the claims in a single document. Since Powell et al. fails to disclose each and every element of the invention methods, as defined by amended claim 65, Applicants respectfully submit that the Examiner has failed to establish anticipation under 35 U.S.C. § 102 (b) over Powell et al. Accordingly, reconsideration and withdrawal of the rejection are respectfully requested.

B. Applicants also respectfully traverse the rejection of claims 65-69 under 35 U.S.C. § 102(b) as allegedly being anticipated by Weaver et al. (U.S. Patent No. 5,055,390). Applicants have canceled claim 66 without prejudice, rendering the rejection moot as pertains to claim 66. Applicants respectfully submit that the invention methods for obtaining an organism from a mixed population of organisms in a sample, as defined by amended claim 65 (and claims 66-69), distinguish over the disclosure of Weaver et al. by requiring:

“encapsulating two or more organisms obtained from the sample, each in a microenvironment suitable for growth of the organisms;

incubating the encapsulated two or more organisms under such conditions and for such a time to allow at least one of the organisms to grow;

sorting the microenvironments by a flow cytometer on growth of the organisms alone to separate organisms that grow under the conditions from organisms that do not grow under the conditions; and

obtaining an organism from grows under the conditions.”

It should be noted that Applicants’ claims do not require secretion or production of any analyte as the basis of cell separation.

By contrast, Weaver et al. disclose methods for fusing the contents of microdroplets in a *non-aqueous environment* to accomplish chemical manipulation of contents of microdroplets by introducing substances, such as tracers (Col. 27, lines 8-50) into one set of the microdroplets. Alternatively, Weaver et al. disclose only capturing of molecules at binding sites in gel microdroplets, such as molecules that are released from biological entities within the microdroplets. When Weaver considers incubation of “entities” within the microdroplets, it is for the purpose of allowing the entities “to produce and secrete molecules . . . thereby resulting in capture of more molecules at binding sites within such GMDs” (Col. 29, lines 25-33). Thus, Weaver et al. fail to disclose encapsulating organisms within a microenvironment suitable for organism growth, incubating the organisms under conditions suitable for such growth, and then sorting the encapsulated organisms using a flow cytometer to separate microenvironments on growth of the organisms alone to separate organisms that grow under the incubation conditions from organisms that do not grow under the incubation conditions. Thus, Weaver et al. fail to disclose each and every element of claims 65-69.

Anticipation under 35 U.S.C. § 102(b) requires that the reference recite each and every element of the claims in a single document. Since Weaver et al. fails to disclose each and every element of the invention methods, as defined by amended claim 65, Applicants respectfully submit that the Examiner has failed to establish anticipation under 35 U.S.C. § 102 (b) over Weaver et al. Accordingly, reconsideration and withdrawal of the rejection are respectfully requested.

C. Applicants also respectfully traverse the rejection of claims 65-70 under 35 U.S.C. § 102(b) as allegedly being anticipated by Thompson et al. (U.S. Patent No. 5,824,485). Applicants have canceled claim 66 without prejudice, rendering the rejection moot as pertains to claim 66. Applicants respectfully submit that the invention methods for obtaining an organism from a mixed population of organisms in a sample, as defined by amended claim 65 (and claims 67-70 dependent therefrom), distinguish over the disclosure of Thompson et al. by requiring:

“individually encapsulating two or more organisms obtained from the sample, each in an aqueous microenvironment suitable for growth of the organism;

incubating the encapsulated organisms under such conditions and for such a time to allow at least one of the organisms to grow; and

sorting the microenvironments by a flow cytometer on growth of the organisms alone to separate organisms that grow under the conditions from organisms that do not grow under the conditions; and

obtaining an organism that grows under the conditions.”

By contrast, Thompson et al. fail to disclose sorting gel microdroplets by a flow cytometer to obtain a native organism from the sample on the of growth of the organism alone, i.e., to separate organisms that grow under the incubation conditions from those that do not grow under the incubation conditions. In fact, Applicants submit that Thompson et al. describe screening “combinatorial gene libraries” in host organisms to determine a product secreted from a host organism. Thus, as the Examiner acknowledges (Office Action, page 13), Thompson speaks of native organisms from environmental samples as “donor organisms useful for preparing a combinatorial gene expression library.”

Applicants submit that Thompson et al are absolutely silent regarding use of gel microdroplets (or any other type of microenvironment) and flow cytometry as a means of sorting native organisms to distinguish between those that have grown during incubation

*in vitro* from those that have not. Thus Thompson et al. fail to disclose each and every element of claims 65 and 67-69.

Anticipation under 35 U.S.C. § 102(b) requires that the reference recite each and every element of the claims in a single document. Since Thompson et al. fail to disclose each and every element of the invention methods, as defined by amended claim 65, Applicants respectfully submit that the Examiner has failed to establish anticipation under 35 U.S.C. § 102 (b) over Weaver et al. Accordingly, reconsideration and withdrawal of the rejection are respectfully requested.

**Rejection Under 35 U.S.C. § 103(a)**

Applicants respectfully traverse the rejection of claims 65-71 under 35 U.S.C. § 103(a) as being unpatentable over the combined disclosures of Thompson et al. (U.S. Patent No. 5,824,485) and Kotitz et al. Applicants have canceled claim 66 without prejudice, rendering the rejection moot as pertains to claim 66. Applicants' remarks above regarding the failure of Thompson to disclose the invention methods apply equally and are incorporated here. In addition, Applicants submit that Thompson et al. fail to suggest the invention methods, as defined by claim 65, or claims 70-71, because Thompson et al. describe construction of libraries of host organisms that are "engineered" to contain one or more sequences from one or more "donor" organisms, including, among others, physiological probes and "chemoresponsive promoters to modulate transcription of a reporter gene only in the presence of a certain kind of activity or a certain class of compounds" (Col. 35, lines 40-56). Applicants submit that Thompson's very emphasis upon chimeric engineered libraries and screening of transfected host cells on the basis of whether the organism secretes a product or interacts in some way with an introduced sequence would lead those of skill in the art away from the simplicity of screening encapsulated native organisms using flow cytometry on the basis of growth of the organism (whether assisted by a magnetic field sensing device or not). Thus, Applicants submit that Thompson et al do not themselves suggest modification of the reference along the lines of



Applicants' invention. Moreover, even if those of skill in the art were motivated by Thompson to modify Thompson's disclosure to arrive at the invention methods, there would be no reasonable expectation of success, especially with respect to organisms obtained from environmental samples. As Applicants teach in the Background of the Specification, most of such organisms have not been successfully cultured in vitro, thus providing those of skill in the art with doubt that a method along the lines of the invention could or would succeed.

Furthermore, Applicants submit that the deficiencies of Thompson for disclosing or suggesting the invention methods, as defined by presently presented claims 65 and 67-71, are not overcome by Kotitz et al. Although Kotitz et al. disclose use of SQUID-based magnetic nanoparticle relaxation measures as a tool for quantitative determination of biological *binding reactions*, Kotitz et al. are silent regarding use of SQUID or any other type of magnetic field sensing device for flow cytometry screening to distinguish between microenvironments, such as gel microdroplets, containing organisms that have grown during incubation in a microenvironment and those containing organisms that did not grow under such conditions.

Thus Applicants submit that *prima facie* obviousness of the invention over Thompson et al. and Kotitz et al., either alone or in combination has not been shown by the Examiner. Accordingly, reconsideration and withdrawal of the rejection under 35 U.S.C. § 103 for alleged lack of patentability are respectfully requested.

### **The Double Patenting Rejection**

A. Applicants respectfully traverse the provisional rejection of claims 65-69 under 35 U.S.C. § 101 as allegedly claiming the same invention as that of claims 1-5 of copending application Serial No. 10/145,281 of copending Application No. US 20030077677 A1 ('677). Applicants have canceled claim 66 without prejudice, rendering the rejection moot as pertains to claim 66. To overcome the rejection, Applicants submit herewith a Terminal Disclaimer disclaiming the terminal portion of any patent that may be granted on the above application that may extend beyond the expiration date of Application No. US 20030077677 A1 ('677).

**B.** Applicants respectfully traverse the provisional rejection of claims 65-71 under 35 U.S.C. § 101 as allegedly claiming the same invention as that of claims 1-5 of copending application Serial No. 10/145,281 of copending Application No. US 20030077677 A1 ('677) in view of Kotitz et al.. Applicants have canceled claim 66 without prejudice, rendering the rejection moot as pertains to claim 66. To overcome the rejection, Applicants submit herewith a Terminal Disclaimer disclaiming the terminal portion of any patent that may be granted on the above application that may extend beyond the expiration date of Application No. US 20030077677 A1 ('677). In addition, Applicants submit that Application No. US 20030077677 A1 ('677) and the present application were co-owned at the filing of the present application. In view of the Terminal Disclaimer filed herein, Applicants submit that Application No. US 20030077677 A1 ('677) is not available as a reference against this application.

Moreover, Applicants respectfully submit that the sole disclosure of Kotitz et al. is not sufficient to disclose or suggest the invention methods for obtaining an organism from a mixed population of organisms in a sample as defined by claims 65 and 67-71. For the reasons presented above, Applicants submit that, despite Kotitz' disclosure pertaining to use of a Super Conducting Quantum Interference Device, Kotitz fails to disclose or suggest a method whereby individually encapsulated organisms in aqueous microenvironments can be grown and then sorted "by a flow cytometer on growth of the organism alone to obtain an organism from a sample that grows under the conditions." Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 65 and 67-71 for alleged obviousness-type double patenting over the combined disclosures of claims 1-5 of US 20030077677 A1 ('677) and Kotitz et. al.

In re Application of:  
Short and Keller  
Application No.: 09/738,871  
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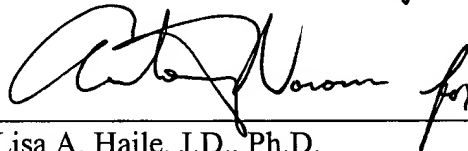
PATENT  
Attorney Docket No.: DIVER1280-6

### CONCLUSION

In summary, for the reasons set forth herein, Applicants maintain that claims 65 and 67-71 clearly and patentably define the invention and respectfully request that the Examiner withdraw all rejections and pass the application to allowance. If the Examiner would like to discuss any of the issues raised in the Office Action, the Examiner is encouraged to call the undersigned so that a prompt disposition of this application can be achieved.

Enclosed is Check No. 573630 in the amount of \$825.00 (\$250.00 for the Notice of Appeal fee, \$65.00 for the Terminal Disclaimer fee, and \$510.00 for the Three (3) Months Extension of Time fee). The Commissioner is hereby authorized to charge for any additional required fees, or credit any overpayments to Deposit Account No. 07-1896.

Respectfully submitted, *Reg. No. 45,517*



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